Amendments to the Claims

Please cancel claims 15, 17-23, 26, 28-35, 39-46 and 49-51 without prejudice or disclaimer to applicants' rights to pursue the subject matter of these claims in this or a related application.

Please amend claims 3, 5, 8-10, 12, 14, 16, 24, 27, 37, 38 and 48 under the provisions of 37 C.F.R. §1.121, as set forth in the Federal Register on June 30, 2003 as follows:

1. (Original) A pharmaceutical composition comprising:

an aqueous carrier;

from 0.1 mg/ml to 20 mg/ml of the composition of a pharmaceutically acceptable salt of

a) a peptide comprising at least 12 and at most 30 consecutive amino acids having a sequence corresponding to

(i) a sequence of amino acids found within a complementarity-determining region (CDR) of a heavy or a light chain of a human monoclonal anti-DNA 16/6 Id antibody, or

(ii) a sequence of amino acids found within a complementarity-determining region (CDR) of a heavy or a light chain of a pathogenic anti-DNA monoclonal antibody that induces a systemic lupus erythematosus (SLE)-like disease response in mice, or

b) a peptide comprising consecutive amino acids having the sequence

(i) TGYYX$_1$X$_2$X$_3$X$_4$X$_5$QSPEKSLEWIG (SEQ ID NO:11)
wherein X$_1$ is Met, Ala or Val; X$_2$ is Gln, Asp, Glu or Arg; X$_3$ is Trp or Ala; X$_4$ is Val or Ser; and X$_5$ is Lys, Glu or Ala;

(ii) EINPSTGGX$_6$X$_7$X$_8$X$_9$X$_{10}$X$_{11}$X$_{12}$KAKAT (SEQ ID NO:12)
wherein X$_6$ and X$_7$ are each Thr, Val or Ala; X$_8$ is Tyr or Phe; X$_9$ is Asn or Asp; X$_{10}$ is Gln or Glu; X$_{11}$ is Lys or Glu, and X$_{12}$ is Phe or Tyr;

(iii) YYCARX$_{13}$X$_{14}$X$_{15}$X$_{16}$PYAX$_{17}$X$_{18}$YWGQGS (SEQ ID NO:13)

wherein X_{13} is Phe, Thr or Gly; X_{14} is Leu, Ala or Ser; X_{15} is Trp or Ala; X_{16} is Glu or Lys; X_{17} is Met or Ala, and X_{18} is Asp, Lys or Ser;

(iv) $GYNX_{19}X_{20}X_{21}X_{22}X_{23}X_{24}SHGX_{25}X_{26}LEWIG$ (SEQ ID NO:14)

wherein X_{19} is Met or Ala; X_{20} is Asn, Asp or Arg; X_{21} is Trp or Ala; X_{22} is Val or Ser; X_{23} is Lys or Glu; X_{24} is Gln or Ala; X_{25} is Lys or Glu, and X_{26} is Ser or Ala;

(v) $YYCARX_{27}X_{28}X_{29}YGX_{30}X_{31}X_{32}GQTL$ (SEQ ID NO:15)

wherein X_{27} is Ser or Phe; X_{28} is Gly or Ala; X_{29} is Arg, Ala or Glu; X_{30} is Asn or Asp; X_{31} is Tyr or Phe, and X_{32} is Trp, His or Ala;

(vi) $X_{33}YYWSWIX_{34}QX_{35}PX_{36}X_{37}GX_{38}EWIG$ (SEQ ID NO:16)

wherein X_{33} is Gly or Thr Gly; X_{34} is Arg or Lys; X_{35} is Pro or Ser; X_{36} is Gly or Glu; X_{37} is Lys or Asp; and X_{38} is Glu, Leu or Ser;

(vii) $YYCARX_{39}LLX_{40}X_{41}X_{42}X_{43}X_{44}DVDYX_{45}GX_{46}DV$ (SEQ ID NO:17)

wherein X_{39} is Gly or Phe; X_{40} is Arg or Ala; X_{41} is Gly or Ala; X_{42} is Gly or Ala; X_{43} is Trp or Ala; X_{44} is Asn or Ala; X_{45} is Tyr or Trp; X_{46} is Met or Gln;

(viii) FSGYYWS (SEQ ID NO:8);

(ix) EINHSGSTNYKTSLKS (SEQ ID NO:9); or

(x) GLLRGGWNDVDYYYGMDV (SEQ ID NO:10), or

c) a peptide comprising consecutive amino acids having a sequence of any of a) and b), or at least two of the sequences in (a)(i), (a)(ii) and (b)(i) through (b)(x), or

d) a peptide comprising consecutive amino acids having a sequence comprising at least two identical sequences included in (a)(i), (a)(ii) and (b)(i)

through (b)(x); and

a solubility enhancer selected from the group consisting of dimethyl-acetamide, polyethylene glycol, polyoxylated castor oil, N-methyl-2-pyrrolidinone, 1-ethenyl-2-pyrrolidinone, polyoxyethylene sorbitan esters, and a substituted β-cyclodextrin,

wherein both the peptide and the solubility enhancer are dissolved in the aqueous carrier; and

wherein the composition has a pH between 4 and 9.

2. (Original) The pharmaceutical composition of claim 1, wherein at least 0.5 mg/ml of the composition is the pharmaceutically acceptable salt of the peptide.

3. (Currently Amended) The pharmaceutical composition of ~~claim 1 or 2,~~ claim 1, wherein the peptide has a sequence selected from the group consisting of:

NH_2- Thr Gly Tyr Tyr Met Gln Trp Val Lys Gln Ser Pro Glu Lys Ser Leu Glu-Trp Ile Gly-COOH (SEQ ID NO:1);

NH_2- Glu Ile Asn Pro Ser Thr Gly Gly Thr Thr Tyr Asn Gln Lys Phe Lys Ala Lys Ala Thr-COOH (SEQ ID NO:2);

NH_2- Tyr Tyr Cys Ala Arg Phe Leu Trp Glu Pro Tyr Ala Met Asp Tyr Trp Gly Gln Gly Ser-COOH (SEQ ID NO:3);

NH_2- Gly Tyr Asn Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile Gly-COOH (SEQ ID NO:4);

NH_2- Tyr Tyr Cys Ala Arg Ser Gly Arg Tyr Gly Asn Tyr Trp Gly Gln Thr Leu -COOH (SEQ ID NO:5);

NH_2-Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Glu Glu Trp Ile Gly-COOH (SEQ ID NO:6);

NH_2-Tyr Tyr Cys Ala Arg Gly Leu Leu Arg Gly Gly Trp Asn Asp Val Asp Tyr Tyr Gly Met Asp Val-COOH (SEQ ID NO:7);

NH_2- Phe Ser Gly Tyr Tyr Trp Ser-COOH (SEQ ID NO:8);

NH_2- Glu Ile Asn His Ser Gly Ser Thr Asn Tyr Lys Thr Ser Leu Lys Ser-COOH (SEQ ID NO:9); and

NH2- Gly Leu Leu Arg Gly Gly Trp Asn Asp Val Asp Tyr Tyr Tyr Gly Met Asp Val-COOH (SEQ ID NO:10).

4. (Original) The pharmaceutical composition of claim 1, wherein the peptide comprises consecutive amino acids having the sequence

X_{33}YYWSWIX_{34}QX_{35}P$X_{36}X_{37}$GX_{38}EWIG (SEQ ID NO:16)

wherein X_{33} is Gly or Thr Gly; X_{34} is Arg or Lys; X_{35} is Pro or Ser; X_{36} is Gly or Glu; X_{37} is Lys or Asp; and X_{38} is Glu, Leu or Ser.

5. (Currently Amended) The pharmaceutical composition of ~~any one of claims 1-4,~~ claim 1, wherein the solubility enhancer is a substituted β-cyclodextrin.

6. (Original) The pharmaceutical composition of claim 5, wherein the substituted β-cyclodextrin is a hydroxypropyl, a sulfobutyl ether, or asulfopropyl ether substituted β-cyclodextrin.

7. (Original) The pharmaceutical composition of claim 6, wherein the substituted β-cyclodextrin is a substituted sulfobutyl ether β-cyclodextrin.

8. (Currently Amended) The pharmaceutical composition of ~~any one of claims 1-7,~~ claim 1, wherein the concentration of peptide in solution is at least 1 mg/ml.

9. (Currently Amended) The pharmaceutical composition of ~~any one of claims 1-7,~~ claim 1, wherein the concentration of peptide in solution is at least 2.5 mg/ml.

10. (Currently Amended) The pharmaceutical composition of ~~any one of claims 1-9,~~ claim 1, wherein the composition has a pH between 6.5 and 8.5.

11. (Original) The pharmaceutical composition of claim 10, wherein the composition has a pH between 7.5 and 8.5.

12. (Currently Amended) The pharmaceutical composition of ~~any one of claims 1-11,~~ claim 1, wherein the pharmaceutically acceptable salt is an acetate salt.

13. (Original) The pharmaceutical composition of claim 5, wherein the pharmaceutically acceptable salt is an acetate salt, and the substituted β-cyclodextrin is hepta-(sulfobutyl ether)-β-cyclodextrin.

14. (Currently Amended) A method of alleviating symptoms of systemic lupus erythematosus (SLE) in a human subject comprising administering to the human subject the pharmaceutical composition of ~~any one of claims 1-13~~ claim 1 in an amount effective to alleviate the symptoms of the SLE in the human subject.

15. (Canceled)

16. (Currently Amended) A process for manufacturing the pharmaceutical composition of ~~any one of claims 1-13~~

claim 1, comprising the steps of:

a) preparing a solution of dimethyl-acetamide, polyethylene glycol, polyoxylated castor oil, N-methyl-2-pyrrolidinone, 1-ethenyl-2-pyrrolidinone,polyoxyethylene sorbitan esters, or a substituted β-cyclodextrin in an aqueous carrier at a predetermined concentration;

b) adding a predetermined amount of a pharmaceutically acceptable salt of

1) a peptide comprising at least 12 and at most 30 consecutive amino acids having a sequence corresponding to

(i) a sequence of amino acids found within a complementarity-determining region (CDR) of a heavy or a light chain of a human monoclonal anti-DNA 16/6 Id antibody, or

(ii) a sequence of amino acids found within a complementarity-determining region (CDR) of a heavy or a light chain of a pathogenic anti-DNA monoclonal antibody that induces a systemic lupus erythematosus (SLE)-like disease response in mice,

2) a peptide comprising amino acids having the sequence

(i) $TGYYX_1X_2X_3X_4X_5QSPEKSLEWIG$ (SEQ ID NO:11)

wherein X_1 is Met, Ala or Val; X_2 is Gln, Asp, Glu or Arg; X_3 is Trp or Ala; X_4 is Val or Ser; and X_5 is Lys, Glu or Ala;

(ii) $EINPSTGGX_6X_7X_8X_9X_{10}X_{11}X_{12}KAKAT$ (SEQ ID NO:12)

wherein X_6 and X_7 are each Thr, Val or Ala; X_8 is Tyr or Phe; X_9 is Asn or Asp; X_{10} is Gln or Glu; X_{11} is Lys or Glu, and X_{12} is Phe or Tyr;

(iii) $YYCARX_{13}X_{14}X_{15}X_{16}PYAX_{17}X_{18}YWGQGS$ (SEQ ID NO:13)
wherein X_{13} is Phe, Thr or Gly; X_{14} is Leu, Ala or Ser; X_{15} is Trp or Ala; X_{16} is Glu or Lys; X_{17} is Met or Ala, and X_{18} is Asp, Lys or Ser;

(iv) $GYNX_{19}X_{20}X_{21}X_{22}X_{23}X_{24}SHGX_{25}X_{26}LEWIG$ (SEQ ID NO:14)
wherein X_{19} is Met or Ala; X_{20} is Asn, Asp or Arg; X_{21} is Trp or Ala; X_{22} is Val or Ser; X_{23} is Lys or Glu; X_{24} is Gln or Ala; X_{25} is Lys or Glu, and X_{26} is Ser or Ala;

(v) $YYCARX_{27}X_{28}X_{29}YGX_{30}X_{31}X_{32}GQTL$ (SEQ ID NO:15)
wherein X_{27} is Ser or Phe; X_{28} is Gly or Ala; X_{29} is Arg, Ala or Glu; X_{30} is Asn or Asp; X_{31} is Tyr or Phe, and X_{32} is Trp, His or Ala;

(vi) $X_{33}YYWSWIX_{34}QX_{35}PX_{36}X_{37}GX_{38}EWIG$ (SEQ ID NO:16)
wherein X_{33} is Gly or Thr Gly; X_{34} is Arg or Lys; X_{35} is Pro or Ser; X_{36} is Gly or Glu; X_{37} is Lys or Asp; and X_{38} is Glu, Leu or Ser;

(vii) $YYCARX_{39}LLX_{40}X_{41}X_{42}X_{43}X_{44}DVDYX_{45}GX_{46}DV$ (SEQ ID NO:17)
wherein X_{39} is Gly or Phe; X_{40} is Arg or Ala; X_{41} is Gly or Ala; X_{42} is Gly or Ala; X_{43} is Trp or Ala; X_{44} is Asn or Ala; X_{45} is Tyr or Trp; X_{46} is Met or Gln;

(viii) FSGYYWS (SEQ ID NO:8);

(ix) EINHSGSTNYKTSLKS (SEQ ID NO:9); or

(x) GLLRGGWNDVDYYYGMDV (SEQ ID NO:10), or

3) a peptide comprising consecutive amino acids having a sequence of any of a) and b), or at least two of the sequences in (a)(i), (a)(ii) and (b)(i) through (b)(x), or

4) a peptide comprising consecutive amino acids having a sequence comprising at least two identical sequences included in (a)(i), (a)(ii) and (b)(i) through (b)(x);

c) adjusting the pH of the solution of step b) until the peptide dissolves in the solution; and

d) if necessary, adjusting the pH of the solution of step c) to a pH of 4-9, thereby manufacturing the pharmaceutical composition.

Claims 17-23. (Canceled)

24. (Currently Amended) A composition prepared by the process of ~~any one of claims 16-23~~ claim 16.

25. (Original) A lyophilized pharmaceutical composition comprising from 0.1 mg/ml to 20 mg/ml of the composition of a pharmaceutically acceptable salt of

a) a peptide comprising at least 12 and at most 30 consecutive amino acids having a sequence corresponding to

(i) a sequence of amino acids found within a complementarity-determining region (CDR) of a heavy or a light chain of a human monoclonal anti-DNA 16/6 Id antibody, or

(ii) a sequence of amino acids found within a complementarity-determining region (CDR) of a heavy or a light chain of a pathogenic anti-DNA monoclonal antibody that induces a systemic lupus erythematosus (SLE)-like disease response in mice, or

b) a peptide comprising consecutive amino acids having

the sequence

(i) TGYYX$_1$X$_2$X$_3$X$_4$X$_5$QSPEKSLEWIG (SEQ ID NO:11)
wherein X$_1$ is Met, Ala or Val; X$_2$ is Gln, Asp, Glu or Arg; X$_3$ is Trp or Ala; X$_4$ is Val or Ser; and X$_5$ is Lys, Glu or Ala;

(ii) EINPSTGGX$_6$X$_7$X$_8$X$_9$X$_{10}$X$_{11}$X$_{12}$KAKAT (SEQ ID NO:12)
wherein X$_6$ and X$_7$ are each Thr, Val or Ala; X$_8$ is Tyr or Phe; X$_9$ is Asn or Asp; X$_{10}$ is Gln or Glu; X$_{11}$ is Lys or Glu, and X$_{12}$ is Phe or Tyr;

(iii) YYCARX$_{13}$X$_{14}$X$_{15}$X$_{16}$PYAX$_{17}$X$_{18}$YWGQGS (SEQ ID NO:13)
wherein X$_{13}$ is Phe, Thr or Gly; X$_{14}$ is Leu, Ala or Ser; X$_{15}$ is Trp or Ala; X$_{16}$ is Glu or Lys; X$_{17}$ is Met or Ala, and X$_{18}$ is Asp, Lys or Ser;

(iv) GYNX$_{19}$X$_{20}$X$_{21}$X$_{22}$X$_{23}$X$_{24}$SHGX$_{25}$X$_{26}$LEWIG (SEQ ID NO:14)
wherein X$_{19}$ is Met or Ala; X$_{20}$ is Asn, Asp or Arg; X$_{21}$ is Trp or Ala; X$_{22}$ is Val or Ser; X$_{23}$ is Lys or Glu; X$_{24}$ is Gln or Ala; X$_{25}$ is Lys or Glu, and X$_{26}$ is Ser or Ala;

(v) YYCARX$_{27}$X$_{28}$X$_{29}$YGX$_{30}$X$_{31}$X$_{32}$GQTL (SEQ ID NO:15)
wherein X$_{27}$ is Ser or Phe; X$_{28}$ is Gly or Ala; X$_{29}$ is Arg, Ala or Glu; X$_{30}$ is Asn or Asp; X$_{31}$ is Tyr or Phe, and X$_{32}$ is Trp, His or Ala;

(vi) X$_{33}$YYWSWIX$_{34}$QX$_{35}$PX$_{36}$X$_{37}$GX$_{38}$EWIG (SEQ ID NO:16)
wherein X$_{33}$ is Gly or Thr Gly; X$_{34}$ is Arg or Lys; X$_{35}$ is Pro or Ser; X$_{36}$ is Gly or Glu; X$_{37}$ is Lys or Asp; and X$_{38}$ is Glu, Leu or Ser;

(vii) YYCARX$_{39}$LLX$_{40}$X$_{41}$X$_{42}$X$_{43}$X$_{44}$DVDYX$_{45}$GX$_{46}$DV (SEQ ID NO:17)
wherein X$_{39}$ is Gly or Phe; X$_{40}$ is Arg or Ala; X$_{41}$ is Gly or Ala; X$_{42}$ is Gly or Ala; X$_{43}$ is Trp or Ala; X$_{44}$ is Asn or Ala; X$_{45}$ is Tyr or Trp; X$_{46}$ is Met or Gln;

(viii) FSGYYWS (SEQ ID NO:8);

(ix) EINHSGSTNYKTSLKS (SEQ ID NO:9); or

(x) GLLRGGWNDVDYYYGMDV (SEQ ID NO:10), or

c) a peptide comprising consecutive amino acids having a sequence of any of a) and b), or at least two of the sequences in (a)(i), (a)(ii) and (b)(i) through (b)(x), or

d) a peptide comprising consecutive amino acids having a sequence comprising at least two identical sequences included in (a)(i), (a)(ii) and (b)(i) through (b)(x); and

a solubility enhancer selected from the group consisting of dimethyl-acetamide, polyethylene glycol, polyoxylated castor oil, N-methyl-2-pyrrolidinone, 1-ethenyl-2-pyrrolidinone, polyoxyethylene sorbitan esters, and a substituted β-cyclodextrin.

26. (Canceled)

27. (Currently Amended) A process of lyophilizing the pharmaceutical composition of ~~any one of claims 1-13,~~ claim 1, comprising the steps of:

a) lowering the temperature of the pharmaceutical composition to -40°C;

b) holding the temperature at -40°C for a predetermined time;

c) raising the temperature of the solution to 20°C;

d) holding the temperature at 20°C for a predetermined time; and

e) reducing the pressure and holding the temperature at 20°C for a predetermined time, thereby lyophilizing the pharmaceutical composition.

Claims 28-35. (Canceled)

36. (Original) The process of claim 27, wherein

step a) is performed within 2 hours;

step b) is performed within 3 hours;

step c) is performed over 13 hours and at a pressure of 110μbar;

step d) is performed over 13 hours and at a pressure of 110μbar; and

step e) is performed over 5 hours and the pressure is reduced to 10μbar.

37. (Currently Amended) A lyophilized pharmaceutical composition prepared by the process of ~~any one of claims 27-36~~ claim 27.

38. (Currently Amended) A process of lyophilizing the pharmaceutical composition of ~~any one of claims 1-13,~~ claim 1, comprising the steps of:

a) lowering the temperature of the pharmaceutical composition to -45°C;

b) holding the temperature at -45°C for a predetermined time;

c) raising the temperature of the solution to -20°C;

d) raising the temperature of the solution to 25°C; and

e) holding the temperature at 25°C for a predetermined time, thereby lyophilizing the pharmaceutical composition.

Claims 39-46. (Canceled)

47. (Original) The process of claim 38, wherein

step a) is performed within 6 hours;

step b) is performed within 3 hours;

step c) is performed over 19 hours and at a pressure of 150μbar;

step d) is performed over 13 hours and at a pressure of 150μbar; and

step e) is performed over 8 hours and at a pressure of 150μbar.

48. (Currently Amended) A lyophilized pharmaceutical composition prepared by the process of ~~any one of claims 38-47~~ claim 38.

Claims 49-51. (Canceled)

52. (Original) A packaged pharmaceutical composition comprised of:

a packaging material; and

a predetermined amount of the lyophilized pharmaceutical composition of claim 37 or 48.